**REMARKS**

The Office Action of March 20, 2001 presents the examination of claims 2-10, 12, and 13. Claim 13 is amended. No new matter is inserted into the application.

***Rejection under 35 U.S.C. § 112, first paragraph***

The Examiner maintains the rejection of claims 2-10, 12, and 13 under 35 U.S.C. § 112, first paragraph, for allegedly not being enabled by the specification. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Specifically, the Examiner apparently maintains two arguments in asserting that the present invention is not enabled. Applicants address these arguments in turn below.

*Detection of a single molecule of target nucleic acid*

On page 3, first paragraph, of the outstanding Office Action, the Examiner writes:

> *As seen in the examples, the non-labeled DNA, when present, was present at an amount of no less than 1%. The claimed method, however, places no limitation on the detection method. Accordingly, the claimed method encompasses the detection of but a single molecule of target nucleic acid while in the presence of any quantity of standard DNA.*

In this passage, it appears that the Examiner asserts that the present invention is not enabled because the claims do not place a lower limit on the amount of DNA that may be detected.

Detection of extremely small amounts, the Examiner argues, would require undue experimentation to be practiced by one of skill in the art.

In response to the Examiner's remarks, Applicants add functional language to claim 13 stating that the mutated or polymorphic target DNA is present in an amplifiable amount. Therefore, any amount of DNA that could not be amplified because the amount is too small is excluded from the scope of the claim.

The use of "amplifiable amount" is similar to "effective amount" held to be definite by the CCPA on several occasions. See, In re Halleck, 422 F2d 911 (CCPA 1970); In re Watson, 517 F2d 465 (CCPA 1975); In re Caldwell, 319 F2d 254 (CCPA 1963). In these cases, the Federal Court has held that the term is not objectionable where the amount is not critical, or where one skilled in the art can determine from the disclosure what an effective amount is, or when the effect achieved is recited.

In the instant case, the claim recites that the target DNA is present in an amplifiable amount; in other words, an effective amount that can be amplified. All non-amplifiable amounts are therefore excluded from the scope of the claims. Secondly, the specification clearly discloses that the target DNA may be preferably in an amount of about 1 to 100 µg, although DNA in an amount of less than 1 µg is also capable of being amplified. The point is, however, that methods of doing

PCR are well known in the art. Therefore, it is not outside the skill of the practitioner to determine an amplifiable amount.

For these reasons, Applicants respectfully submit that the claims comply fully with the law as recited under 35 U.S.C. § 112, first paragraph, and as interpreted by the Federal Courts. As such, withdrawal of the instant rejection is respectfully requested.

*Hybridization conditions*

On page 3, third paragraph, of the outstanding Office Action, the Examiner writes:

> *The claimed method requires that the hybridization conditions be such that they would permit "competitive hybridization". Such broad-based conditions do not necessarily preclude non-target yet highly similar sequences [from] being detected.*

In this passage, it appears that the Examiner is asserting that the present invention is not enabled because the claims do not recite hybridization conditions, and therefore the hybridization would produce "background noise" from highly similar sequences.

In response to the Examiner's remarks, Applicants add functional language to claim 13 more fully describing the competitive hybridization. Nevertheless, Applicants make note that it is not undue experimentation for one skilled in the art to determine hybridization conditions, given the guidance provided in the specification. For example, hybridization

conditions "wherein the temperature is reduced from 98°C to 50°C at the rate of 1°C per 3 to 10 minutes" are recited on page 20, second paragraph of the instant specification.

Applicants respectfully submit that the present invention is indeed enabled by the instant specification. For these reasons, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph be withdrawn.

***Summary***

In summary, Applicants submit that all of the present claims define patentable subject matter such that this application should be placed into condition for allowance. Early and favorable action of the merits of the present application is thereby respectfully requested.

If the above amendments for some reason do not place the present application into a condition for allowance, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. No. 45,702) at 703-205-8000 to arrange for a personal interview in order to expedite prosecution of the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and further replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any

additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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**Version To Show Marked Changes:**

13. (Amended) A nucleic acid assay process for identifying and/or quantifying a mutation or polymorphism in a sample DNA, comprising the steps of:

providing [a] labeled standard DNA having a nucleotide sequence the same as a mutated or polymorphic target DNA of interest, wherein said labeled standard DNA comprises a double stranded nucleic acid having a site capable of binding to a solid support on one strand and a detectable label on the other strand;

amplifying a particular region of an analyte nucleic acid which is present in a specimen to prepare a double stranded sample DNA, for competitive hybridization wherein said sample DNA comprises both wild-type and mutated or polymorphic target DNA in an amplifiable amount;

selecting a detection limit for said mutated or polymorphic target DNA, wherein when the detection limit for the target DNA present in said sample DNA is A/B, the excessiveness of said sample DNA is at least B/A, and wherein A/B is the fractional equivalent of the percentage of target DNA content in the sample DNA;

adding an excessive amount of said sample DNA to said labeled standard DNA, to allow competitive hybridization to take place between said target DNA and labeled standard DNA under

conditions which allow for rehybridization of at least some of said labeled standard DNA and under conditions wherein non-target sample DNA does not hybridize with said labeled standard DNA, wherein the excessiveness of said sample DNA added to said labeled standard DNA in the competitive hybridization is selected in accordance with the pre-selected detection limit,

detecting the rehybridized labeled standard DNA by utilizing said detectable label and said site capable of binding to a solid support; and

evaluating the degree of exchange that occurred during competitive hybridization of the complementary strands between said sample DNA and said labeled standard DNA.